

I claim:

1. A GLP-2 formulation comprising:
 - (a) a medically useful amount of a naturally occurring GLP-2 peptide or an analog thereof;
 - (b) a phosphate buffer in an amount sufficient to adjust the pH of the formulation to a physiologically tolerable level;
 - (c) L-histidine; and
 - (d) a bulking agent selected from the group consisting of mannitol and sucrose.

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2. The GLP-2 formulation of claim 1, wherein the pH of the formulation is greater than about 6.0.

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3. The GLP-2 formulation according to claim 2, wherein the pH of the formulation is from about 6.9 to about 7.9.

4. The GLP-2 formulation of claim 3, wherein the pH of the formulation is from about 7.3 to about 7.4.

5. The GLP-2 formulation of claim 1, wherein the GLP-2 peptide or analog thereof is present at a concentration of about 0.1 to about 50 mg/ml.

6. The GLP-2 formulation of claim 5, wherein the GLP-2 peptide or analog thereof is present at a concentration of about 5 to about 40 mg/ml.

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7. The GLP-2 formulation of claim 6, wherein the GLP-2 peptide or analog thereof is present at a concentration of about 7 to about 30 mg/ml.

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8. The GLP-2 formulation of claim 7, wherein the GLP-2 peptide or analog thereof is present at a concentration of about 10 to about 20 mg/ml.

9. The GLP-2 formulation of claim 8, wherein the L-histidine is present in an amount of about 0.5 to about 1%.

10. The GLP-2 formulation of claim 9, wherein the bulking agent is mannitol.

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11. The GLP-2 formulation of claim 10, wherein the mannitol is present at a concentration of about 2 to about 5%.

12. The GLP-2 formulation of claim 11, wherein the mannitol is present at a 10 concentration of about 2.5 to about 3.5%.

13. The GLP-2 formulation of claim 1, wherein the GLP-2 peptide is selected from the group consisting of a mammalian GLP-2 peptide, a vertebrate GLP-2 peptide, and a human GLP-2 peptide.

14. The GLP-2 formulation of claim 13, wherein the GLP-2 peptide has the sequence of a GLP-2 species from n animal selected from the group consisting of a primate, rat, mouse, porcine species, oxine species, bovine species, degu, hamster, guinea pig, fish, chicken, and human.

15. The GLP-2 formulation of claim 14, wherein the GLP-2 peptide is h[Gly2]GLP-2.

16. The GLP-2 formulation of claim 1, wherein the GLP-2 analog is identified by a process comprising:

25 (a) screening peptides against cells genetically engineered to produce the GLP-2 receptor, and
(b) identifying peptides which bind to the GLP-2 receptor, wherein such peptides are identified as GLP-2 peptides useful in the formulation of claim 1.

30 17. The GLP-2 formulation of claim 1, wherein the GLP-2 peptide is an analog of natural GLP-2, the analog having:

10 (a) one or more amino acid substitutions, additions, deletions, or modifications; and
(b) biological activity.

15 18. The GLP-2 formulation of claim 1, wherein the GLP-2 peptide is an analog which
has been altered to confer resistance to endogenous enzymes.

20 19. The GLP-2 formulation of claim 18, wherein the alteration comprises substitution
of the alanine residue at position 2 of GLP-2 with another suitable amino acid.

25 20. The GLP-2 formulation of claim 19, wherein the alanine residue at position 2 is
substituted with glycine or serine.

10 21. The GLP-2 formulation of claim 1, wherein the GLP-2 analog is a GLP-2 receptor
antagonist.

15 22. The GLP-2 formulation of claim 1 in lyophilized form.

20 23. The lyophilized formulations of claim 22, comprising less than about 5% water by
weight.

25 24. The lyophilized formulations of claim 23, comprising 2% or less water by weight.

26 25. The GLP-2 formulation of claim 1, which is stable at ambient temperature for up
to at least 6 months, as evidenced by GLP-2 peptide degradation of less than about 5% during
this time period.

26 26. The GLP-2 formulation of claim 25, wherein less than about 3 to about 4%
peptide degradation is observed after storage of the GLP-2 formulation during the time period.

27. The GLP-2 formulation of claim 26, wherein less than about 1 to about 2% peptide degradation is observed after storage of the GLP-2 formulation during the time period.

28. The GLP-2 formulation of claim 1, which is stable at a temperature of about 4°C for up to at least 18 months, as evidenced by GLP-2 peptide degradation of less than about 5% during this time period.

29. The GLP-2 formulation of claim 28, wherein less than about 3 to about 4% peptide degradation is observed after storage of the GLP-2 during the time period.

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30. The GLP-2 formulation of claim 29, wherein less than about 2% peptide degradation is observed after storage of the GLP-2 formulation during the time period.

11 31. A GLP-2 formulation comprising:

- (a) about 0.1 to about 50 mg/ml of a GLP-2 peptide or an analog thereof;
- (b) a phosphate buffer in an amount sufficient to adjust the pH of the formulation to a pharmaceutically tolerable level;
- (e) about 0.5 to about 1% L-histidine; and
- (f) about 2 to about 5% mannitol.

20 32. The GLP-2 formulation of claim 31, wherein the GLP-2 is h[Gly2]GLP-2.

33. The GLP-2 formulation of claim 32, wherein the formulation is lyophilized.

25 34. The GLP-2 formulation of claim 32, wherein the pH of the formulation is selected from the group consisting of greater than about 6.0, and from about 6.9 to about 7.9.

35. The GLP-2 formulation of claim 34, wherein the pH of the formulation is from about 7.3 to about 7.4.

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36. A method for making a lyophilized formulation of GLP-2 comprising the following steps:

- (a) preparing a GLP-2 formulation comprising:
 - (i) a GLP-2 peptide or an analog thereof;
 - (ii) a phosphate buffer in an amount sufficient to adjust the pH of the formulation to a pharmaceutically tolerable level;
 - (iii) L-histidine; and
 - (iv) a bulking agent selected from the group consisting of mannitol and sucrose;
- (b) freezing the formulation to -40°C;
- (c) drying the formulation in a first drying step at -20°C; and
- (d) drying the formulation in a second drying step at +20°C.

37. The method of claim 36, wherein the pH of the GLP-2 formulation prior to freezing is selected from the group consisting of greater than about 6.0, and from about 6.9 to about 7.9.

38. The method of claim 37, wherein the pH of the formulation is from about 7.3 to about 7.4.

39. The method of claim 36, wherein the freezing process of step (b) comprises:

- (a) cooling the formulation from ambient temperature to about -1°C at about 2°C/minute, followed by maintaining the formulation at about -1°C for about 15 minutes; and
- (b) cooling the formulation from about -1°C to about -40°C at about 2°C/minute, followed by maintaining the formulation at about -40°C for about 4 hours.

40. The method of claim 36, wherein the drying process of step (c) comprises:

- (a) raising the temperature from about -40°C to about -20°C at about 2°C/minute; and

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(b) maintaining the formulation at about -20°C for about 14 hours under a vacuum of about 150 mT with a condenser temperature of about -80°C.

41. The method of claim 36, wherein the drying process of step (d) comprises:

(a) warming the formulation from about -20°C to about +20°C at about 2°C/minute;

(b) maintaining the formulation at about +20°C for about 14 hours at a vacuum of about 150 mT and a condenser temperature of about -80°C until there is less than about 5% of water remaining in the formulation.

42. The method of claim 41, wherein the formulation is maintained at about +20°C, at a vacuum of about 150 mT and a condenser temperature of about -80°C, until there is no more than about 2% of water remaining in the formulation

43. A kit comprising:

(a) a lyophilized GLP-2 formulation comprising:

(i) a GLP-2 peptide or an analog thereof;

(ii) a phosphate buffer in an amount sufficient to adjust the pH of the formulation to a pharmaceutically acceptable level;

(iii) L-histidine; and

(iv) a bulking agent selected from the group consisting of mannitol and sucrose;

(b) a vial of sterile water for reconstitution; and

(c) instructions directing reconstitution.

44. The kit of claim 43, wherein the pH of the GLP-2 formulation is selected from the group consisting of greater than about 5.5, greater than about 6.0, and from about 6.9 to about 7.9.

45. The kit of claim 44, wherein the pH of the formulation is from about 7.3 to about

7.4.

46. The kit of claim 43 further comprising an injection device for administration.

5 47. The kit of claim 43, wherein following reconstitution the GLP-2 formulation is stable for at least about 12 hours.

10 48. The kit of claim 43, wherein following reconstitution the GLP-2 formulation is stable for up to about 24 hours.

15 49. A method for treating a human or animal having a disorder, disease or condition for which treatment with GLP-2 is indicated, the method comprising the step of administering a therapeutically effective amount of a GLP-2 formulation comprising:

- (a) a GLP-2 peptide or an analog thereof;
- (b) a phosphate buffer in an amount sufficient to adjust the pH of the formulation to a pharmaceutically tolerable level;
- (c) L-histidine; and
- (d) a bulking agent selected from the group consisting of mannitol and sucrose.

20 50. The method of claim 49, wherein the pH of the GLP-2 formulation is selected from the group consisting of greater than about 5.5, greater than about 6.0, and from about 6.9 to about 7.9.

25 51. The method of claim 50, wherein the pH of the formulation is from about 7.3 to about 7.4.

52 The method of claim 49, wherein the GLP-2 treatment is for gastrointestinal disease.

30 53. The method of claim 49, wherein the GLP-2 formulation is administered by injection.

54. The method of claim 49, wherein the GLP-2 formulation is administered by infusion.